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Nasal Carriage of *Staphylococcus aureus* and Antistaphylococcal Immunoglobulin E Antibodies in Atopic Dermatitis

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Twelve atopic dermatitis patients were studied to investigate the relationship between levels of antistaphylococcal immunoglobulin E antibodies in serum and quantitative cultures of *Staphylococcus aureus* strains from the anterior nares and chronic lesions. A positive correlation was found between logarithmic counts of *S. aureus* strains from the anterior nares and levels of antistaphylococcal immunoglobulin E in serum. The observation is important for understanding the pathophysiology of atopic dermatitis.

Atopic dermatitis is often associated with a family history of atopy (6). The skin of patients with atopic dermatitis exhibits a striking susceptibility to colonization and infection with *Staphylococcus aureus*. This organism is present in up to 100% of exudative lesions and in up to 91% of chronic lichenified plaques (8). A pathophysiological role of *S. aureus* in the intense pruritus and subsequent scratching and excoriations which characterize atopic dermatitis has been proposed (3). The recent observation of increased levels of antistaphylococcal immunoglobulin E (IgE) antibodies (SIgEs) in the serum of these patients provides further evidence for this relationship (1, 9, 11). In an attempt to determine the possible correlation between total IgE and SIgE levels and *S. aureus* colonization, we have carried out quantitative cultures of *S. aureus* cells taken from the skin and anterior nares of 12 atopic dermatitis patients.

Twelve consecutive atopic dermatitis patients seen in the Dermatology Clinic of Children's Hospital of Philadelphia were entered in the study. These patients had the following characteristics: (i) family history of atopy; (ii) history of atopic dermatitis for 1 to 15 years; (iii) recent exacerbation of skin disease. We excluded from the study patients who had received systemic or oral antibiotics or steroids in the preceding 3 months. All patients in the study were using emollients on their skin. The most afflicted skin showed erythema, oozing, vesiculation, and crusting. Other areas of dermatitis showed lichenification and slight scaling.

Quantitative cultures for *S. aureus* were done on dry, lichenified plaques lacking exudation or any sign of infection. Bacteriological samples were obtained by a detergent scrub technique (12). Briefly, this was done by scrubbing a total of 2 ml of 0.1% polysorbate 80 solution for 2 min into a sterile cup held adherent to the skin. Cultures of the anterior nares were done by three clockwise and three counterclockwise rotations of a sterile swab in each nasal passage. At the start and between nasal passages the swab was dipped in 2 ml of 0.1% polysorbate 80 solution and finally left in the test tube after its proximal end was broken off and discarded. Single drops (0.025 ml) from a 10-fold dilution series were plated on Trypticase soy agar (BBL Microbiology Systems) and Trypticase soy agar with lecithin and polysorbate 80. The plates were incubated aerobically at 35°C for 2 days. The total number of *S. aureus* CFU per square centimeter was then determined. In addition to cultures of diluted suspensions, cultures of undiluted suspensions were also made. Single drops of each 10-fold dilution were inoculated from a vertical 0.2-ml bacteriological pipette. Such drops contain approximately 0.025 ml and are more uniform in volume and surface-spreading characteristics than are water, broth, or saline. *S. aureus* organisms were identified as colonies consisting of pigmented, coagulase-positive staphylococci.

The total IgE level in serum was measured by the Phadebus radioimmunosorbent test (Pharmacia, Inc., Piscataway, N.J.) (5). Briefly, paper disks are covalently bound with anti-human IgE and incubated for 3 h with serum from the patient. Unbound IgE is removed by washing the disks with 0.9% saline solution. The disks are incubated for 18 h with ^{125}I-labeled anti-human IgE. After washing, radioactivity is recorded; the amount of activity bound to the disk is directly proportional to the concentration of IgE in serum.

Whole organisms of *S. aureus* wood 46 were used as a solid-phase reactant for determination of antistaphylococcal IgE by the method developed in our laboratory (9). Bacteria were cultured for 18 h in brain heart infusion broth, centrifuged at 900 × *g* for 10 min, and washed twice with phosphate-buffered saline solution. They were then suspended in a phosphate-buffered saline solution containing 0.5% sodium azide. The final bacterial concentration in the suspension was 8.5×10^9 organisms per ml. Aliquots (1 ml) of the bacterial suspension were centrifuged, and the pellet was incubated at 25°C with 0.05 ml of serum from the patient for 3 h with constant stirring. The pellet was washed three times to remove unbound IgE and incubated for 18 h with 0.05 ml (0.8 Ci/ml) of ^{125}I-labeled equine anti-human IgE (Kallestad). Unbound anti-human IgE was then removed by washing twice in phosphate-buffered saline, and the radioactivity of the bacterial pellet was recorded. Results are expressed as the percent total activity of added ^{125}I-labeled anti-human IgE. Positive and negative controls consisted of sera from patients with the hyper-IgE syndrome and healthy volunteers, respectively.

Table 1 describes the results of cultures and total and SIgE levels in our patients. All the patients except one had cultures positive for *S. aureus* in both skin and anterior nares. There was no correlation between the counts of *S. aureus* on the skin or anterior nares and the total IgE level. However, when the logarithm of *S. aureus* counts in the

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TABLE 1. *S. aureus* colonization, SIgE levels, and total IgE levels in sera of 12 untreated patients with atopic dermatitis

Patient no.	Age (yr)	Duration of disease (yr)	*S. aureus* density (10^3 CFU/cm^2) in:		SIgE binding (%)	Total IgE (IU/ml)
			Skin	Anterior nares		
1	14	10	224	251	2.0	400
2	14	13	6,864	1,585	5.5	5,000
3	2	1	119	0.63	0.8	25
4	2	2	1,000	3,981	6.6	3,900
5	1	1	53	1.2	0.8	800
6	5	2	40	631	4.2	1,000
7	15	9	106	158	2.2	2,000
8	15	15	30	1,195	7.4	3,500
9	3	2	0[a]	0[a]	0.8	20
10	10	5	1,320	6,309	8.5	15,000
11	2	1	92	10	1.5	1,000
12	5	2	50	1,259	6.3	550

[a] No *S. aureus* colonies were detected after plating 0.025 ml of an undiluted suspension.

anterior nares was plotted against the logarithm of the SIgE level, a positive correlation was demonstrated ($r = 0.968$) (Fig. 1). There was no correlation between SIgE levels and counts of *S. aureus* on the skin. No correlation was present between SIgE levels and the age of the patients or the duration of their disease.

The recent observation of elevated SIgE levels (1) in patients with atopic dermatitis has led to several hypotheses about the pathophysiological role of SIgE in the clinical manifestations. Attachment of IgE to tissue basophils and mast cells may cause the release of mediators in the presence of *S. aureus* antigens. These mediators may lead to impaired neutrophil chemotaxis and thus to increased susceptibility of atopic dermatitis skin to colonization with *S. aureus* (1). *S. aureus* colonization of the anterior nares and of involved skin in patients with atopic dermatitis is very common, reaching an incidence of 79 and 93%, respectively, in one study (2).

In this study we chose to culture lichenified plaques and the anterior nares. We excluded obviously infected areas because we decided that the oozing and crusting present in these lesions was due to chronic scratching and excoriations.

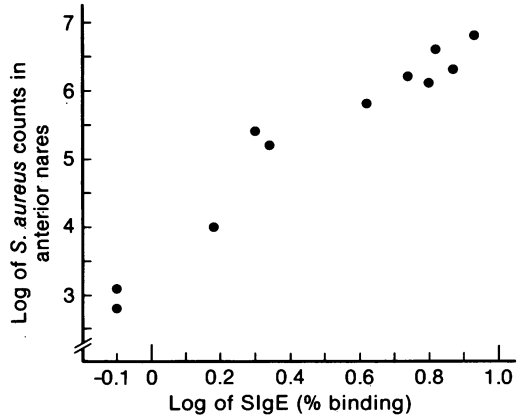

FIG. 1. Correlation of the logarithm of the mean *S. aureus* CFU ± standard deviation in the anterior nares (5.3 ± 1.4) and SIgE levels (0.49 ± 0.38); $r = 0.968$.

SIgE levels correlated with *S. aureus* counts in the anterior nares but not with those in the skin. This observation may be explained by the anatomical nature of the anterior nares, which are an identifiable limited site that may be representative of the *S. aureus* burden. Quantitative nasal cultures from carriers of *S. aureus* have yielded a bacterial log mean of 5.146 (13), which is remarkably similar to the number of organisms found in our patients. SIgE levels were not significantly elevated in normal individuals tested thus far (1, 9–11), but in these studies nasal cultures for *S. aureus* were not obtained. Future investigators will have to determine whether increases in SIgE levels occur in normal individuals harboring *S. aureus* in their anterior nares. Lacking such data, we must indicate that the correlation we observed between *S. aureus* counts and SIgE levels in this study may not be specific for patients with atopic dermatitis. No statement may be made about the activity of the atopic dermatitis and the presence of *S. aureus* and SIgE in our study since, as we described in the methods, all our patients were experiencing an exacerbation of their skin condition.

It was our intent to repeat the cultures and determine the SIgE levels after systemic antibiotic treatment. However, in three of four patients studied after systemic antibiotic treatment, the level of SIgE increased markedly despite a reduction in *S. aureus* counts in samples from the skin and anterior nares. Table 2 shows the results of cultures and SIgE determinations in these four patients after 2 weeks of therapy with erythromycin stearate (40 mg/kg per day in four divided doses). In all four cases the *S. aureus* organisms recovered were susceptible to erythromycin. We could not find any differentiating clinical features in patient no. 3, in whom the level of SIgE did not increase. Only minimal improvement in the dermatitis was noted in these four patients while on no other treatment but the systemic antibiotics. We interpreted the finding of increased SIgE levels after antibiotic treatment as possibly secondary to a release of *S. aureus* antigens. However, Jarrett (7) suggested that IgE responses may occur only when the amount of antigen is below a threshold required to stimulate IgE-suppressor T cells. Measurement of SIgE levels by using purified cell walls rather than whole organisms (4, 10) may lead to a better understanding of this particular phenomenon. However, we do feel that the present method, involving the use of whole organisms as the immunosorbent, is an acceptable way of studying SIgE levels (1, 9–11).

In summary, we have found a positive correlation between SIgE levels and *S. aureus* counts in the anterior nares in a group of patients with active atopic dermatitis. This observation may provide a framework for further investigations of the pathophysiological role of *S. aureus* and SIgE.

TABLE 2. *S. aureus* colonization, SIgE levels, and total IgE levels in four treated patients with atopic dermatitis

Patient no.	*S. aureus* density (10^3 CFU/cm^2) in:		SIgE binding (%)	Total IgE (IU/ml)
	Skin	Anterior nares		
1	184	15	13	575
3	0	0.5	0.8	19
4	25	0	8.2	3,900
7	92	0	5	800
Mean ± SD	75 ± 82	3.9 ± 7.4	6.7 ± 5.1	1,323 ± 1,749

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